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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
LUCAS, ZACHARIAH

ART UNIT	PAPER NUMBER
1648	12

DATE MAILED: 07/30/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/839,894	ALTBOUM ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- Th MAILING DATE of this communication appears on th cov r she t with the correspondenc addr ss --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 June 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-81* is/are pending in the application.

4a) Of the above claim(s) *2-9, 17-34, 36-47, and 51-81* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,10-16,35, and 48-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 April 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☒ Interview Summary (PTO-413) Paper No(s). *12* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Interview Summary

1. Attached to this action, the applicant should find an interview summary of the telephonic interview between the examiner, supervisory examiner Housel, and the applicant's attorney James J. Mullen III. The applicant should note that the box that excuses the applicant from submitting a separate record of the interview is checked. It has been checked because the Applicant's Supplemental Response is an adequate summary of the interview.

Election/Restrictions

2. Applicant's election without traverse of Group I, and of Group E in Paper No. 11 is acknowledged.

3. Claims 2-9, 17-34, 36-47, and 51-81 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 11

4. It should be here noted that although the invention D is described as "drawn to SEQ ID NO: 9 or a sequence encoding SEQ ID NO: 10," because the elected invention is a polypeptide, invention D should be read as to a polypeptide of SEQ ID NO: 10, or a polypeptide encoded by SEQ ID NO: 9. This does not affect the claims elected.

Specification

5. The disclosure is objected to because of the following informalities:

On page 6, line 2; the specification reads, in part, as follows: "a product that is at least 95% homologous to *anyone* of these ..." (italics added). The "anyone" should read as "any one."

On page 6, line 19; the term embodiment should be in the plural form.

On page 26, line 6; the reference to Chang states that the article is on page 615, whereas it is disclosed in the IDS (properly) as on pages 617-624; and, on line 18; the Hitzeman reference is on page 12073, rather than page 2073.

Appropriate correction is required.

Drawings

6. The drawings are objected to because although the brief description of Figure 2 mentions the "*parA* and *parM*" plasmid partitioning system, figure 2 shows only "*par*" and "*parM*" on the described plasmid. A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1, 10-11, 35, and 48-50 are rejected under 35 U.S.C. 102(b) as being anticipated by McConnell et al., Infection and Immunity, 56:1974-1980 (McConnell), and Rudin et al, Microbial Pathogenesis, 16:131-139 (Rudin) These claims describe an immunogenic composition comprising a aA

McConnell teaches that CS4 expressing E. coli were able to produce antibodies to CS4. p. 1975. Because the article discloses the entire CS4 as an immunogen, it also inherently discloses an immunogenic composition comprising the CsaE subunit. Further, McConnell also teaches the same *csa* operon as is disclosed by the specification. On page 9 of the specification, the applicant states that the operon of the application "was cloned from ETEC Eii881A, a CS4 producer strain." On page 1976, in Table 1 of the McConnell, the reference discloses that E11881A is a ETEC strain producing CS4. Thus, McConnell teaches not only any *csa* operon product, but also the specific one described in the specification.

Rudin also teaches that CS4 is immunogenic. P. 134-35. Like McConnell, Rudin also does not teach specific immunogenic subunits of CS4, however as it teaches use of the whole, it also inherently includes composition comprising the CsaE subunit.

The references anticipate the claims, because while they disclose only the use of the entire CS4 fimbriae, the immunogen taught by them falls within the scope of the claims. In the specification, the applicant states that an example of a carrier component "is the CS4 antigen, which is encoded by the *csa* operon." P. 32, lines 7-8. The applicant also states:

> Carrier components that possess both mucosa binding characteristics and immunogenic characteristic may be used. For example, in one embodiment, the CsaB and/or the CsaE proteins can function both as the carrier component and the immunogenic component.

Specification, p. 32, lines 26-29. Together, these two statements indicate that a recombinant CS4 antigen may be both immunogen and the carrier, thereby indicating that the claims read on any recombinant CS4 fimbriae that can stimulate an immune reaction.

The fact that neither reference specifically identifies that any of the antigens used therein are made by recombinant means does not prevent anticipation. The applicant has not shown that the source of the peptides has any effect on their structures. Because of this, the term recombinant in the claims is not seen as limiting, and therefore has no affect on the anticipatory effect of the references.

9. Claims 1, 12-15, and 35 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 96/38171, naming Cassels et al. as inventors (Cassels). Claim 1 describes an immunogenic composition comprising a recombinant product of a *csa* operon and a carrier. Claim 35 describes a purified polypeptide sequence expressed from a recombinant *csa* operon or an antigenic fragment thereof.

Cassels discloses a CS4 fragment that is usable as an immunogen. Pp. 4, line 8. The fragment disclosed by the reference appears, by comparison with the sequences in the case file, to be identical, with the exception of a single conservative substitution, to residues 24-60 of SEQ ID NO: 4 (CsaB). Because the claims allow for some variance of the polypeptide structure, and because the applicants have not indicated that the source (recombinant or otherwise) of the peptide has any effect on its structure or function, and because the peptide disclosed by Cassels is inherently a product of a *csa* operon, the peptide fragment anticipates the identified claims.

Cassels further states that the vaccine compositions comprising the polypeptides disclosed therein may be introduced into a patient by any conventional means, "including

parenteral routes (subcutaneous, intradermal, intramuscular) and by direct application to mucous membranes. Lyophilized composition may be "snorted" into the nasal cavity." P. 5, lines 14-18. The reference also teaches the encapsulation of the peptides according to U.S. Patent Number 5,417,986, which teaches encapsulation of peptides in such a manner that they are able to reach, and be absorbed by, the intestines without being broken down by the digestive tract. See, Patent 5,417,986, cols. 3-4. Thus, the reference teaches that the peptide may be in a composition suitable for any method of administration.

10. Claim 16 is rejected under 35 U.S.C. 102(b) as anticipated by McConnell or, in the alternative, under 35 U.S.C. 103(a) as obvious over McConnell, in view of U.S. Patent Number 5,932,715, issued to Scott et al (Scott); or optionally in view of Lodish et al., excerpt from a Molecular Cell Biology text (Lodish), and further in view of Scott. Claim 16 reads on an immunogenic composition comprising a recombinant product of a *csa* operon wherein the product is an expression vector.

The teachings of McConnell are described, in part, above. The reference also identifies a plasmid containing the operon. Pp. 1976-1977. Because the *csa* operon is on a plasmid, and plasmids are commonly used as expression vectors, the McConnell reference teaches an expression vector comprising the *csa* operon. Because the applicant has not described any structural of functional distinction between a recombinant expression vector and a naturally occurring plasmid, the term recombinant is not limiting. Thus, McConnell anticipates the claim. However, even if the operon was not on a plasmid, it is known in the art to make expression vectors to express proteins. See, e.g. Lodish, pp. 252-254. Even if McConnell did not teach a

plasmid, the fact that it tells how to identify the nucleotides coding for CS4 would allow one of ordinary skill in the art to make an expression vector.

Scott teaches an immunogenic composition including recombinant CS2 proteins. Col. 4, lines 11-15. The patent teaches that recombinant CS2 pili may be obtained by culturing host cells transformed with the recombinant polynucleotides comprising sequences encoding the CS2. Col. 4, lines 56-60. Further, Scott also teaches that the disclosed vaccine could be advantageously combined with antigens of other fimbriae, including CS4. Col. 4, lines 20-23. From this reference, it would be obvious to one of ordinary skill in the art to make a vaccine comprising a CS4 immunogen made by a recombinant method wherein a *csa* nucleotide was expressed by a cell transformed by a vector containing the nucleotide. This reference provides both a motivation (the advantageous combination of antigens), and a reasonable expectation of success (the fact that CS2 antigens were successful), for the combination of itself with a reference teaching CS4, and in particular with references teaching a CS4 vector. Thus, these references render claim 16 obvious.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 12-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over McConnell in view of Cassels. For the purposes of this rejection, the claims are being read as to the immungenic compositions of claims 12-15 wherein the peptides are those taught by McConnell. The teachings of both McConnell and Cassels are described above.

From these references, it would have been obvious to one of ordinary skill in the art to prepare compositions of the claimed peptides suitable for the types of administration described by the claims. This is because both McConnell and Cassels are teaching the use of peptides derived from the same as immunogenic compounds to the same diseases. It would therefore have been obvious to one of ordinary skill in the art to use the routes of administration taught by Cassels for the peptides taught by McConnell. There would have been a reasonable expectation of success due to the fact that Cassels described the use of those methods for peptides similar to the McConnell peptides both in structure and in purpose. There would have been no reason to expect that the methods of Cassels would not have worked for larger peptides than the fragments described by Cassels.

Conclusion

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 703-308-4240. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the

organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Z. Lucas
Patent Examiner
July 22, 2002